proteus
DIGITAL HEALTH

February 22, 2019

VIA ELECTRONIC FILING

Ms. Marlene H. Dortch
Secretary
Federal Communications Commission
445 12th Street, S.W.
Washington, D.C. 20554

Re: Written *Ex Parte* Communication
WC Docket No. 18-213

Dear Ms. Dortch:

On behalf of Proteus Digital Health®, Inc. (Proteus), a cutting-edge healthcare company headquartered in Redwood City, California, I am writing to introduce the Commission to Proteus' work in "digital medicines," and to highlight its implications for patient well-being and reducing healthcare costs. Proteus' efforts dovetail with the Commission's interest in and leadership with respect to the intersection of communications, technology, and healthcare. Indeed, as noted by Chairman Pai, "[b]roadband-enabled telehealth services . . . can significantly improve Americans' health and reduce costs for patients and health care providers alike."[1] Commissioner Carr observed that "[r]emote technologies – whether enabled by a smartphone, tablet, or other device – are bringing high-quality, affordable care to communities across the country."[2] Likewise, as emphasized in the statement of Commissioner Geoffrey Starks before the U.S. Senate Committee on Commerce, Science and Transportation, "[t]elehealth practices are already revolutionizing the way in which doctors can provide care and treatment."[3] Digital medicines are emblematic of these truths.

Proteus also has an interest in the Commission's "Connected Care" *Notice of Inquiry* in WC Docket No. 18-213, and, for the reasons set forth below, urges the Commission to (1)

[1] Separate Statement of Chairman Ajit Pai, *Promoting Telehealth for Low-Income Consumers*, Notice of Inquiry, 33 FCC Rcd 7825, 7846 (2018).
[2] Separate Statement of Commissioner Brendan Carr, *Promoting Telehealth for Low-Income Consumers*, Notice of Inquiry, 33 FCC Rcd 7825, 7850 (2018) ("Carr Statement").
[3] Written Statement for the Record of Geoffrey A. Starks, Nominee, Federal Communications Commission, U.S. Senate Committee on Commerce, Science and Transportation (June 20, 2018), https://www.commerce.senate.gov/public/_cache/files/8e09c601-94f5-4a51-b0d1-1ae2b9fede7a/AB7D65A01A5F23D83C5CC009071CBA88.06-18-18starks-testimony.pdf.

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ensure that projects featuring use of digital medicines are eligible for funding under the Connected Care pilot program, and (2) continue to promote broadband connectivity in unserved and underserved areas, an effort that is necessary if we are to see optimal use of telehealth applications.

BACKGROUND

Studies have shown that at least 50% of prescribed medications are not taken as directed.[4] Medication non-adherence in turn leads to uncontrolled health conditions, excess hospitalizations, emergency room trips and office visits. Furthermore, if doctors don't know if their patients are taking their medications, they can only guess as to whether those patients need an altered dose or a different medication. All of this has a substantial economic impact: according to a recent study in the Annals of Pharmacotherapy, inappropriate drug use costs the U.S. more than $500 billion a year, representing about 16% of total healthcare spending.[5]

Proteus is spearheading the development of a new type of pharmaceutical: digital medicines (also known as DigiMeds™). Specifically, Proteus developed an Ingestible Event Marker (IEM) sensor (roughly the size of a grain of salt and coated in minerals found in the human diet), which is embedded in a patient's medication and communicates after it has been swallowed. Among other things, the sensor enables close monitoring of medication-taking patterns and thereby allows a healthcare provider or caregiver to determine whether a patient is following his or her medication regimen.

The benefits of this model are manifest. A patient using digital medicines receives regular feedback about his or her medication-taking behaviors. With permission, the digital medicines program also shares information with the patient's healthcare team to ensure that the patient is receiving the full value of his or her prescriptions. For the healthcare team, digital medicines improve patient outcomes by measuring ingestions and providing data that leads to improved clinical decision-making and patient engagement. Most important, patients stay healthier with better outcomes, don't need to see their doctors as often, avoid hospitalizations, and enjoy an improved quality of life. Collectively, these benefits have the potential to substantially reduce healthcare costs. Not coincidentally, Proteus' extensive clinical trial and commercial experience with digital medicines has been overwhelmingly positive. Proteus has consistently shown that patients who use DigiMeds take them about 90% of the time, a figure substantially higher than the take-rate for regular drugs.[6] Additionally, physicians coach patients and properly titrate medicines at three times the normal rate when they have the data

[4] *See, e.g.,* Proteus Digital Health®, Inc. Press Release, "Proteus Digital Health® Announces Digital Medicines Pipeline Development and Expansion into Oncology" (Apr. 25, 2018) ("Proteus April 25, 2018 Press Release"), https://www.proteus.com/press-releases/proteus-digital-health-announces-digital-medicines-pipeline-development-and-expansion-into-oncology/.
[5] *Id.*
[6] *Id.*

that Proteus's solutions provide.[7] A representative list of publications reaffirming the benefits of Proteus's technology is attached hereto as Exhibit 1.

In November 2017, the Food and Drug Administration (FDA) issued the first approval of a digital medicine system using Proteus' technology.[8] The system, called ABILIFY MYCITE®, is a drug-device combination product comprised of Abilify tablets manufactured by Otsuka Pharmaceutical Co., Ltd. (Otsuka) and embedded with the IEM developed by Proteus. Abilify is an antipsychotic drug used to treat adults with various mental illnesses. The ABILIFY MYCITE system also includes the MYCITE® Patch (a wearable sensor developed by Proteus); the MYCITE® APP, a smartphone application that displays information for the patient on compatible smartphones; and web-based portals for healthcare providers and caregivers. The system works as follows:

- The IEM activates when in contact with stomach fluid and communicates with the MYCITE Patch.

- The MYCITE Patch detects and records the date and time of the ingestion of the tablet, as well as certain physiological data such as patient activity level, and communicates all of this information to the MYCITE APP on a compatible mobile device.

- The MYCITE APP allows individuals to review their objective medication ingestion and daily activity level, as well as enter their mood and rest. They can also invite others to view their data.

- The web-based portals give healthcare providers and caregivers the ability to display the patient's drug ingestion patterns over time, as well as the patient's daily activity level and self-reported mood and rest. With this information in hand, physicians and their care teams are better equipped to quickly decode patterns around medication adherence and patient behaviors; make objective decisions about when to initiate, titrate or eliminate medication; and optimize treatment therapies, allowing patients to more quickly reach their treatment goals.

Beyond MYCITE, Proteus aggressively pursued expansion of its portfolio of digital medicines. In April 2018, Proteus announced that, together with its collaborators, it had developed a pipeline of 31 digital medicines for mental health, cardiovascular and metabolic conditions, infectious diseases, and oncology.[9] For example, with respect to infectious disease, the company announced that it had developed seven digital medicines used in clinical studies

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[7] *Id.* Titration is the process of adjusting the dosage of medication that a patient is taking.

[8] *See, e.g.,* Proteus Digital Health®, Inc. Press Release, "Otsuka and Proteus® Announce the First U.S. FDA Approval of a Digital Medicine System: Abilify MyCite® (aripiprazole tablets with sensor)" (Nov. 17, 2017), https://www.proteus.com/press-releases/otsuka-and-proteus-announce-the-first-us-fda-approval-of-a-digital-medicine-system-abilify-mycite/.

[9] Proteus April 25, 2018 Press Release.

to treat patients with tuberculosis, hepatitis C, and HIV.[10] For patients with cardiovascular and metabolic conditions, Proteus announced that it had developed a panel of 15 digital medicines.[11] Proteus conducted several clinical studies demonstrating the clinical and economic benefits of digital medicines for these types of patients, including a successful randomized control trial involving patients with uncontrolled hypertension and type 2 diabetes.

The expansion of Proteus' DigiMeds portfolio into oncology is especially beneficial for rural patients. Chairman Pai, citing findings by the Centers for Disease Control and Prevention, noted that rural Americans are more likely to die of cancer than their urban counterparts.[12] As pointed out by Dr. Linda Sutton, an associate professor at the Duke University School of Medicine and an adviser to Proteus' oncology program, "[t]he explosion of therapeutic options with new drugs, as well as new molecular and genetic tests, has made oncology care increasingly complicated. We need the ability to support patient use of drugs in the right dose, on the right schedule, and ensure that these powerful medications are working as intended… With digital oral chemotherapy, the patient's oncologist is in a better position to determine if subsequent problems are related to disease progression or drug toxicity, and better able to assess drug efficacy."[13]

More recently, in October 2018, Proteus and Otsuka announced that they entered into an expanded global collaboration agreement for further development and commercialization of digital medicines, including ABILIFY MYCITE.[14] This includes the joint development of an expanded portfolio of digital medicines consisting of therapies such as atypical antipsychotics integrated with Proteus sensors. Proteus and Otsuka will also work on the joint development of next generation product features and sensor capabilities to expand the potential of digital medicine offerings.

RECOMMENDATIONS

As Commissioner Carr put it,"[g]iven the significant cost savings and improved patient outcomes associated with connected care, we should align public policy in support of this

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[10] *Id.*

[11] *Id.* Proteus has since expanded this panel to include more than 20 digital medicines for patients with cardiovascular and metabolic conditions. *See* Proteus Digital Health®, Inc. Press Release, "Digital Medicines Value-Based Contract Focused on Improving Patient Outcomes Established Between Desert Oasis Healthcare and Proteus Digital Health®" (Aug. 14, 2018), https://www.proteus.com/press-releases/digital-medicines-value-based-contract-focused-on-improving-patient-outcomes-established-between-desert-oasis-healthcare-and-proteus-digital-health/.

[12] Remarks of Chairman Ajit Pai, Connected Health Conference, Boston, MA (October 18, 2018), https://www.fcc.gov/document/chairman-pai-discusses-fccs-telehealth-work-boston-conference.

[13] Proteus April 25, 2018 Press Release.

[14] Proteus Digital Health®, Inc. Press Release, "Otsuka and Proteus Digital Health Announce Expanded Collaboration Agreement to Advance Digital Medicines" (Oct. 11, 2018), https://www.proteus.com-/press-releases/otsuka-and-proteus-digital-health-announce-expanded-collaboration-agreement-to-advance-digital-medicines-for-mental-health/.

movement in telehealth."[15] Proteus agrees, and thus supports the Commission's leadership in raising awareness about the benefits of and need for greater use of technology in healthcare, much of which is dependent on communications technology (wireline and wireless).

Further, Proteus is particularly interested in the Commission's Connected Care *Notice of Inquiry*, in which the Commission proposes to launch a $100 million pilot program to promote the use of broadband-enabled telehealth services among low-income families and veterans.[16] In the notice, the Commission observed that "studies show that remote patient monitoring . . . has the potential to significantly improve health outcomes."[17] This is precisely the case with digital medicines, and Proteus has substantial clinical results that prove the point. In addition, "[b]eyond better health outcomes, telehealth technologies also offer the promise of significantly reducing health care costs."[18] This is also true of digital medicines.

Digital medicines also can benefit low-income patients. First, by providing a mechanism for self-monitoring of medication intake, digital medicines improve patient health and thereby reduce or eliminate the costs low-income patients would ordinarily have to pay for additional hospitalizations and office visits. Second, because digital medicines allow healthcare providers to monitor a patient's medication intake remotely via the web, low-income patients may consult with their physicians on medication issues without having to travel (which is particularly beneficial for those low-income patients living in rural areas who do not have local physicians nearby). Third, as low-income Americans become increasingly reliant on smartphones to access the Internet, Proteus' mobile-friendly technology will provide them with a readily-accessible tool that will help ensure that they are taking their medications properly.[19]

Digital medicines also hold great promise for treating veterans. For example, Commissioner Carr noted how, in the case of one Navy veteran, remote monitoring of his blood pressure dramatically reduced office visits and allows his doctors to intervene if his blood pressure readings are out of range.[20] Regulation of blood pressure medication via digital medicines can have a similarly beneficial effect on veterans (and other patients) with chronic hypertension. Digital medicines can also be especially useful for treating post-traumatic stress disorder and other mental health conditions, where incorrect use of medication can lead to hospitalization.

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[15] Remarks of Commissioner Brendan Carr, University of Mississippi Medical Center Event on the FCC's Connected Care Pilot Program (July 13, 2018), https://docs.fcc.gov/public/attachments/DOC-352655A1.pdf.

[16] *Promoting Telehealth for Low-Income Consumers*, Notice of Inquiry, 33 FCC Rcd 7825 (2018) ("*Connected Care NOI*").

[17] *Id.* at 7827 (footnote omitted).

[18] *Id.* at 7829

[19] *See* Pew Research Center, "Mobile Fact Sheet" (Feb. 5, 2018) ("Reliance on smartphones for online access is especially common among younger adults, non-whites and lower-income Americans."), http://www.pewinternet.org/fact-sheet/mobile/.

[20] Carr Statement, 33 FCC Rcd at 7850.

Accordingly, while Proteus supports the Commission's commitment to funding broadband connectivity via the Connected Care pilot program, it urges the Commission to take particular note of pilot proposals that include digital medicines in their "toolbox" of telehealth applications that will run over those broadband connections. As the Commission conducts policy in this arena, it should be willing to consider all telehealth innovations in the marketplace (including digital medicines), and promote their use. Acknowledgement of the value of digital medicines also would be consistent with the program's focus on delivering broadband-enabled telehealth services and applications to low-income patients outside of brick-and-mortar health care facilities, while achieving the program's fundamental objective of improving patient outcomes. Moreover, in the *Notice of Inquiry* the Commission asks how the Connected Care pilot program can "improve health care affordability for low-income Americans and counteract the burdens of increasing out-of-pocket expenses, including transportation costs for rural and remote patients."[21] For the reasons discussed above, inclusion of digital medicines in Connected Care pilots will help achieve the Commission's cost-saving objectives as well.

Lastly, Proteus supports the Commission's ongoing efforts to promote broadband deployment to unserved and underserved areas, whether through the Connected Care pilot program or otherwise.[22] It is beyond argument that telehealth solutions need broadband connections in order to operate effectively and efficiently. Identifying and eliminating broadband coverage gaps will help unleash the full potential of telehealth for all Americans.

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Proteus looks forward to working with the Commission on telehealth matters in the future. Please contact me if you have any questions regarding this submission.

Sincerely,

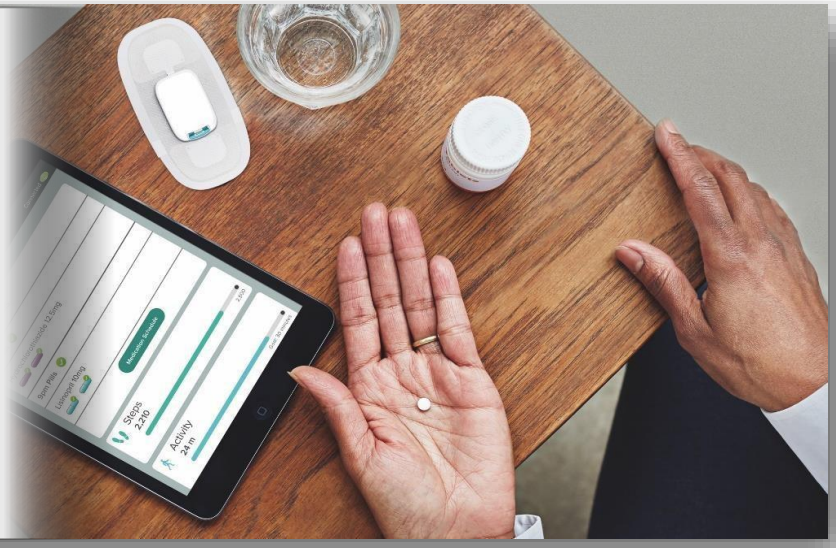
/s/

George M. Savage, M.D.
Co-Founder & Chief Medical Officer

[21] *Connected Care NOI*, 33 FCC Rcd at 7833 (footnote omitted).
[22] *Id.* at 7834.

EXHIBIT 1

Digital Medicines: Highest Impact Publications to Date



Digital Medicines as a new category of pharmaceutical therapy are supported in the literature by over 100 (~110) publications (both published abstracts and manuscripts). The dozen most impactful peerreviewed published manuscripts are delineated below with full-text to follow. These publications span cardiovascular, infectious disease, and mental health therapeutic areas representing collectively over a thousand patients. The key findings include:

- Proven accuracy and safety of the Proteus technology in diverse populations: ○ Extensively studied across diverse patient populations (i.e. various diseases, geographies, ages, races, and income levels) prior to obtaining FDA clearance (492 persons, 6,407 wearable sensor-days, and 20,993 ingestible sensors)
    - ○ ≥ 97.3% of ingested sensors detected with 100% correct identification; no false positives
    - ○ No serious adverse events
- Improved clinical outcomes in patients with hypertension and other CV risk factors: ○ Significantly reduced blood pressure, glycated hemoglobin (A1C), and LDL-C in patients with comorbid, uncontrolled hypertension and type 2 diabetes resistant to drug therapy
    - ○ 98% of ‘drug refractory‘patients achieved BP goal using digital medicines in 12 weeks
- Overall average adherence of approximately 86% during the first 4-12 weeks of Proteus use. ○ Adherence in patients being treated for Hepatitis C with digital DAAs persists around 94% in patients with risk factors for poor compliance.
- Nearly equivalent outcomes demonstrated among patients with mental illness, spanning patients of all ages from children to elderly, with or without co-morbidity, irrespective of sociodemographic status or living situation.

These publications include both pragmatic studies and randomized clinical trials with cohorts of >100 patients enrolled, as well as meta-reviews describing safety and efficacy in thousands of patients on aggregate, with more than 180,000 ingestions recorded to date.

High Impact Publications:

- Frias J, Virdi N, Raja P, Kim Y, Savage G, Osterberg L. Effectiveness of Digital Medicines to Improve Clinical Outcomes in Patients with Uncontrolled Hypertension and Type 2 Diabetes: Prospective, Open-Label, Cluster-Randomized Pilot Clinical Trial. J Med Internet Res 2017;19(7):e246.

- Hafezi H., Robertson T., Moon G., Au-Yeung K., Zdeblick M., Savage G. An Ingestible Sensor for Measuring Medication Adherence. IEEE Transactions on Biomedical Engineering, 2014; 00.00: 1-24

- Plowman RS, Peters-Strickland T, Savage GM Digital medicines: clinical review on the safety of tablets with sensors. Expert Opinion on Drug Safety. Aug 2018; 17:9, 849-852

- Au-Yeung KY, Moon GD, Robertson TL, et al. Early clinical experience with a networked system for promoting patient self- management. American Journal of Managed Care 2011; 17: 277-287.

- Noble et al. Medication adherence and activity patterns underlying uncontrolled hypertension: Assessment and recommendations by practicing pharmacists using digital health care. JAPHA 2016;56:310- 315.

- Moorhead P, Zavala A, Kim Y, Virdi N. Efficacy and safety of a medication dose reminder feature in a digital health offering with the use of sensor-enabled medicines. JAPHA 2017; 57:155-161

- Au-Yeung K, DiCarlo LA. Cost comparison of wirelessly versus directly observed therapy for adherence confirmation in tuberculosis treatment. International Journal of Tuberculosis and Lung Disease 2012; 16: 1498-1504

- Belknap R, Weis S, Brookens A, Au-Yeung KY, Moon G, et al. Feasibility of an ingestible sensor-based system for monitoring adherence to tuberculosis therapy. PLoS ONE 2013; 8(1): e53373.doi:10.1371/journal.pone.0053373

- Profit D, Rohatagi S, Zhao C, Hatch A, Docherty J, Peters-Strickland T. Developing a Digital Medicine System in Psychiatry: Ingestion Detection Rate and Latency Period. J Clin Psychiatry. 2016;77(09):e1095-e1100

- Peters-Strickland T, Pestreich L, Hatch A, Rohatagi S, Baker RA, Docherty J, Markovtsova, Raja P, Weiden P, Walling D. Usability of a novel digital medicine system in adults with schizophrenia treated with sensor-embedded tablets of aripiprazole. Neuropsychiatr Dis Treat. 2016;12:2587-2594.

- Naik R, Macey N, West RJ, Godbehere P, Thurston SC, Fox R, Xiang W, Kim Y, Singh I, Le adley S, and DiCarlo L. First Use of an Ingestible Sensor to Manage Uncontrolled Blood Pres sure in Primary Practice: The UK Hypertension Registry. J Community Med Health Educ 201 7, 7:1.